

CLAIMS

I Claim:

- 1 1. An implantable sensor for sensing a concentration of an organic
2 substrate, the sensor comprising:
3 a conductive electrode; and
4 a stabilized enzyme emulsion in contact with the electrode, the enzyme
5 emulsion comprising:
6 an enzyme that quantitatively oxidizes the organic substrate;
7 a water immiscible oxygen dissolving compound emulsified into
8 intimate contact with the enzyme to provide oxygen; and
9 a protein crosslinking agent to crosslink and insolubilize the
10 enzyme forming a stabilized gel comprising crosslinked
11 protein and particles of the oxygen dissolving substance.
- 1 2. The implantable sensor of Claim 1 further comprising a
2 semipermeable membrane covering the electrode with the enzyme emulsion sandwiched
3 between the membrane and the electrode.
- 1 3. The implantable sensor of Claim 1, wherein the enzyme emulsion
2 also contains an additional carrier protein.

1 4. The implantable sensor of Claim 3, wherein the additional carrier
2 protein is selected from the group consisting of serum albumin and, gelatin.

1 5. The implantable sensor of Claim 1, wherein the oxygen dissolving
2 substance is selected from the group consisting of perfluorocarbons, silicone oils,
3 fluorosilicone oils, aromatic and aliphatic hydrocarbon oils or solids, carotenoids and
4 steroids.

1 6. The implantable sensor of Claim 5, wherein the oxygen dissolving
2 substance is a perfluorocarbon liquid selected from the group consisting of perfluorooctyl
3 bromide, perfluorodichlorooctane, perfluorodecalin, perfluoroindane, perfluoro-
4 phenanthrene, perfluorotetramethylcyclohexane, perfluoropolyalkylether oil, perfluoro-
5 methyldecalin, perfluorodimethylethylcyclohexane, perfluorodimethyldecalin, perfluoro-
6 trimethyldecalin, perfluoroisopropyldecalin, perfluoropentamethyldecalin, perfluoro-
7 diisopropyl decalin, perfluorodiethyldecalin, perfluoromethyladamantane, perfluoro-
8 dimethyladamantane, perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.

1 7. The implantable sensor of Claim 1, wherein the crosslinking agent
2 is selected from the group consisting of aldehydes, carbodiimides, imidoesters,
3 pyrocarbonates, epoxides and N-hydroxysuccinimid esters.

1 8. The implantable sensor of Claim 1, wherein the oxidase enzyme is
2 selected from the group consisting of cholesterol oxidase, amino acid oxidase, alcohol
3 oxidase, lactic acid oxidase, oxygen oxidoreductase, galactose oxidase, and glucose
4 oxidase.

1 9. The implantable glucose sensor of Claim 1 further comprising an
2 electron transport compound dissolved in the perfluorocarbon liquid.

1 10. The implantable glucose sensor of Claim 9, wherein the electron
2 transport compound comprises ferrocene.

1 11. The implantable sensor of Claim 1, wherein the enzyme emulsion
2 further comprises an antioxidant.

1 12. The implantable sensor of Claim 1, wherein the enzyme emulsion
2 further comprises an antimicrobial agent.

1 13. The implantable sensor of Claim 1, wherein the enzyme emulsion
2 further comprises an anti-inflammatory agent selected from the group consisting of
3 steroids, lymphokines, and non-steroidal anti-inflammatory drugs.

1 14. An implantable glucose sensor for sensing a concentration of
2 glucose, the sensor comprising:

3 a metal electrode; and

4 a stabilized enzyme emulsion in contact with the electrode, the enzyme
5 emulsion comprising:

6 a solution of glucose oxidase protein for oxidizing glucose to
7 quantitatively produce hydrogen peroxide;

8 a perfluorocarbon liquid emulsified with the glucose oxidase; and

9 a crosslinking agent to crosslink covalently said protein to form a
10 stabilized gel comprising crosslinked protein and particles of the
11 perfluorocarbon liquid.

1 15. The implantable glucose sensor of Claim 14 further comprising a
2 semipermeable membrane covering the electrode with the enzyme emulsion in contact
3 with a first surface of the membrane and sandwiched between the membrane and the
4 electrode and with body fluids or cells in contact with a second surface of the semi-
5 permeable membrane.

1 16. The implantable sensor of Claim 14, wherein the oxygen
2 dissolving substance is selected from the group consisting of perfluorocarbons, silicone
3 oils, fluorosilicone oils, aromatic and aliphatic hydrocarbon oils or solids, carotenoids
4 and steroids.

1 17. The implantable sensor of Claim 16, wherein the oxygen
2 dissolving substance is a perfluorocarbon liquid selected from the group consisting of
3 perfluorooctyl bromide, perfluorodichlorooctane, perfluorodecalin, perfluoroindane,
4 perfluorophenanthrene, perfluorotetramethylcyclohexane, perfluoropolyalkylether oil,
5 perfluoromethyldecalin, perfluorodimethylethylcyclohexane, perfluorodimethyldecalin,
6 perfluorotrimethyldecalin, perfluoroisopropyldecalin, perfluoropentamethyldecalin,
7 perfluorodiisopropyl decalin, perfluorodiethyldecalin, perfluoromethyladamantane,
8 perfluorodimethyladamantane, perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.

1 18. The implantable glucose sensor of Claim 14 further comprising an
2 electron transport compound dissolved in the perfluorocarbon liquid.

1 19. The implantable glucose sensor of Claim 18, wherein the electron
2 transport compound comprises ferrocene.

1 20. A method for producing a stabilized enzyme emulsion for use with
2 a polarographic or amperometric sensor comprising the steps of:
3 making an aqueous solution of a water soluble enzyme that oxidizes an
4 organic substrate to produce hydrogen peroxide;
5 emulsifying a volume of a water immiscible oxygen dissolving substance
6 into the aqueous solution to form an emulsion;
7 contacting the emulsion with a protein crosslinking agent; and
8 spreading a mixture of the protein crosslinking agent and the emulsion
9 into a uniform layer whereby the emulsion becomes crosslinked to
10 form a solid gel.

1 21. The method of Claim 20, wherein to the emulsion is contacted with
2 a carrier protein prior to contacting with the protein crosslinking agent.

1 22. The method of Claim 21, wherein the aqueous solution contains
2 the carrier protein and the water soluble enzyme is added to the emulsion prior to
3 contacting with the protein crosslinking agent.

1 23. The method of Claim 20, wherein the oxygen dissolving substance
2 is selected from the group consisting of perfluorocarbons, silicone oils, fluorosilicone
3 oils, aromatic and aliphatic hydrocarbon oils or solids, carotenoids and steroids.

1 24. The method of Claim 23, wherein the oxygen dissolving substance
2 is a perfluorocarbon liquid selected from the group consisting of perfluorooctyl bromide,
3 perfluorodichlorooctane, perfluorodecalin, perfluoroindane, perfluorophenanthrene,
4 perfluorotetramethylcyclohexane, perfluoropolyalkylether oil, perfluoromethyldecalin,
5 perfluorodimethylethylcyclohexane, perfluorodimethyldecalin, perfluorotrimethyldecalin,
6 perfluoroisopropyldecalin, perfluoropentamethyldecalin, perfluorodiisopropyl decalin,
7 perfluorodiethyldecalin, perfluoromethyladamantane, perfluorodimethyladamantane,
8 perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.

1 25. A method for producing a stabilized enzyme emulsion for use with
2 a polarographic sensor comprising the steps of:
3 making an aqueous solution of a carrier protein;
4 emulsifying a volume of a perfluorocarbon liquid into the aqueous
5 solution to form an emulsion;
6 contacting the emulsion with a water soluble enzyme that oxidizes an
7 organic substrate to produce hydrogen peroxide to form a mixture;
8 contacting the mixture with a protein crosslinking agent; and
9 spreading a mixture of the protein crosslinking agent and the emulsion
10 into a uniform layer whereby the emulsion becomes crosslinked to
11 form a solid gel.

- 1 26. The method of Claim 25, wherein the oxygen dissolving substance
2 is a perfluorocarbon liquid selected from the group consisting of perfluorooctyl bromide,
3 perfluorodichlorooctane, perfluorodecalin, perfluoroindane, perfluorophenanthrene,
4 perfluorotetramethylcyclohexane, perfluoropolyalkylether oil, perfluoromethyldecalin,
5 perfluorodimethylethylcyclohexane, perfluorodimethyldecalin, perfluorotrimethyldecalin,
6 perfluoroisopropyldecalin, perfluoropentamethyldecalin, perfluorodiisopropyl decalin,
7 perfluorodiethyldecalin, perfluoromethyladamantane, perfluorodimethyladamantane,
8 perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.